REMARKS

Claims 3 and 16 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite.

Of course, the enantiomers are stereoisomers of the monoterpene ketone itself. While it is believed this is apparent, the word "thereof" has been inserted at two places in claim 3.

The dependency of claim 16 has been corrected.

The present invention as defined by presently amended claim 1 concerns a transdermal therapeutic system comprising nicotine as drug and containing spearmint oil, the dominant constituents of which are monoterpene ketones, or at least one monoterpene ketone contained in spearmint oil, wherein the content of the at least one monoterpene ketone in the nicotine-containing layer or zone is 0.1 to 5.0%-wt. The spearmint oil acts as an absorbefacient, i.e., an agent causing absorption, and also highly effectively masks the odor of the nicotine.

The rejections of claims 1, 2 and 14 under 35 U.S.C. 102(b) as being anticipated by Yamaguchi et al, claims 1, 2, 5 and 15 under 35 U.S.C. 102(b) as being anticipated by Majeti, claims 1-5, 14 and 15 under 35 U.S.C. 103(a) as being unpatentable over Yamaguchi et al and Majeti in view of Baker et al and claims 6-8 and 16 under 35 U.S.C. 103(a) as being unpatentable over Yamaguchi et al and

Majeti and Baker et al in view of Brisken et al and DeFoney et al are respectfully traversed.

Yamaguchi et al. (US 5,820877) teach percutaneously administrable patch preparations which may be used to administer nicotine to assist in quitting smoking (col. 4, line 18). It is further specified that the drug storage layer of the patches may contain, among others, absorbefacients (col.4, line 51). Mentha oil and 1-menthol are disclosed to be absorbefacients that may be contained in the patch (col.4, lines 51-52). Mentha oil is supposed to be mint oil (Oleum Menthae arvensis), the dominant constituents of which are monoterpene alcohols, especially menthol. Thus, the present invention differs from the teaching of Yamaguchi et al with respect to the relevant compounds. In addition, Yamaguchi et al do not teach the amount of absorbefacient that may be contained in their patch nor are monoterpene ketones disclosed to be suitable absorbefacients.

Majeti teaches transdermal or transmucosal administration forms for the treatment of nicotine craving or smoking withdrawal symptoms. Although it is mentioned that the composition of Majeti's invention may contain aromatic components, it is apparent that in fact only the transmucosal administration forms contain flavoring agents (example 2; claims 7 and 8). Example 1 teaches that transdermal delivery systems are not supposed to contain flavors.

Furthermore, neither spearmint oil nor monoterpene ketones are named as suitable aromatic components (col. 6, lines 6 to 18). Preferred aromatic components according to Majeti are aldehydes and alcohols, but monoterpene ketones are not mentioned at all.

In summary, neither the disclosure of Yamaguchi et al nor that of Majeti anticipates any of the present claims.

The Baker reference relates to methods and therapeutic systems for smoking cessation. Baker et al disclose transdermal therapeutic systems with a backing layer, at least one layer containing nicotine and a removable protective layer. Baker at al also discloses another embodiment, namely nicotine lozenges and further specifies that flavorants could be added to a nicotine lozenge to mask the taste of nicotine (col. 20, lines 26-32) or even contain tobacco flavor to reproduce the sensation of smoking (col. 20, lines 37-39). It was already conceded in the International Preliminary Examination Report that the use of a flavorant in a transdermal therapeutic system is not considered in this reference, although transdermal therapeutic systems are extensively discussed. The use of flavorants is restricted solely to oral administration forms.

Furthermore, menthaceous essential oils are named as flavorants among others such as chocolate, vanilla or tobacco which would definitely not be suitable to improve the odor of a nicotine-containing transdermal therapeutic system.

Among the menthaceous essential oils menthol was named to be a suitable flavorant. However, the experimental data provided in the present application demonstrates the superiority of monoterpene ketones over menthol. It was surprisingly found by the applicant that monoterpene ketones such as menthone or carvone have properties superior to monoterpene alcohols and that spearmint oil is better than mint oil and peppermint oil (page 6, 1st and 2nd paragraph; Figure 1) in masking an unpleasant odor from a nicotine-containing transdermal therapeutic system. Such a particular suitability of monoterpene ketones and their superiority over monoterpene alcohols could not be inferred from the Baker reference.

Further, the Baker reference does not provide any information regarding the amounts of flavorants which are necessary to mask the taste of nicotine in a lozenge. In contrast, the present application provides thoroughly evaluated amounts of monoterpene ketones that are preferably to be used in order to improve the odor of a nicotine-containing patch. The mere listing of some flavorants which may be added to a nicotine lozenge is believed not to be sufficient to make obvious to those with ordinary skill in the art that particular amounts of monoterpene ketones are preferably suitable to improve the odor of a nicotine-containing transdermal system.

Moreover, there is no motivation in the references to combine them as suggested by the Examiner. Yamaguchi et al. teach the use of l-menthol or

mentha oil as absorbefacients. This indicates that the monoterpene alcohols within the mentha oil serve as absorbefacients. Neither Yamaguchi et al nor Baker et al mention that monoterpene ketones may serve as absorbefacients in transdermal therapeutic systems. Thus, there is no suggestion by Yamaguchi et al in view of Baker et al to use monoterpene ketones in order to improve the odor of transdermal therapeutic systems containing nicotine.

It should be appreciated that the inventor surprisingly found out that monoterpene alcohols and mint oil are less suitable for achieving the object of the present invention than monoterpene ketones and spearmint oil. The superiority of monoterpene ketones and spearmint oil over monoterpene alcohols and mint oil could not be inferred from the cited references.

In addition, none of the references teaches any amount of monoterpene ketones being suitable or preferred for masking the odor of nicotine in a transdermal therapeutic system.

The Baker reference as well as the Majeti reference teach the use of flavors or aromatic components for oral administration forms containing nicotine. The oral administration form can be a lozenge or capsule (Baker et al, col. 20, lines 26-32; Examples 33-35) or a "buccal dosage form" in the form of a plaster (Majeti, example II). Neither of these references teaches transdermal therapeutic systems that comprise a flavorant or odor masking substance.

In addition, it should be considered that the disclosure of Majeti regarding the amount of flavorants in the transmucosal administration form is rather confusing. According to col. 6, 2nd paragraph, aromatics may be present at a level from about 0.0001 % to about 1 %, preferably from about 0.001 % to about 1 %, and most preferably from about 0.001 % to about 0.5 %. These ranges are well below the preferred range of monoterpene ketones within the nicotine-containing layer of the inventive transdermal therapeutic systems. However, claim 8 specifies the amount of flavorants in the tranamucosal carrier being from 0.01 % to about 5 %, and Example II discloses an amount of 10 %-wt of flavorant in the drug reservoir. Hence, the disclosure of Majeti is unclear regarding suitable amounts of a flavorant for transmucosal dosage forms and does not provide the skilled artisan with an idea of suitable amounts for monoterpene ketones in transdermal therapeutic systems to mask the odor of nicotine.

The process for masking the unpleasant odor of a nicotine-containing transdermal therapeutic system was rejected as being unpatentable over any one of the above mentioned references in view of Brisken et al and DeFoney at al. Brisken et al teach a process for the manufacture of a smoking product and the use of odor masks such as menthol (col. 7, line 4), whereas DeFoney et al disclose pharmaceutically acceptable odor masking substances in encapsulated form present

in a capsule (abstract). However, the disclosure of Brisken et al and of DeFoney et al concern "oral administration forms".

Hence, Baker et al, Majeti, Brisken et al, and DeFoney et al teach the use of flavorant in connection with oral admlnlstration forms. In particular menthol is used to provide a good taste for the patient himself. These references do not provide any information regarding the use of flavorants in administration forms intended for external application such as transdermal therapeutic systems and applicant therefore believes that any combination of these references did not make the present invention obvious to the skilled artisan.

Mentha oil or 1-menthol are used as absorbefacients in unknown amounts in transdermal therapeutic systems according to Yamaguchi et al. Yamaguchi does not address the problem that a nicotine-containing patch might possess an unpleasant smell and neither Brisken et al nor DeFoney et al indicates that monoterpene ketones are suitable to mask the odor of nicotine in a nicotine-containing patch.

It is, therefore, believed the application is now in condition for allowance and that action is earnestly solicited.

Respectfully submitted,

Jordan and Hamburg LLP

By _____
C. Bruce Hamburg
Reg. No. 22,389
Attorney for Applicants

Jordan and Hamburg LLP
122 East 42nd Street
New York, New York 10168
(212) 986-2340

APPENDIX I

AMENDED CLAIMS WITH AMENDMENTS INDICATED THEREIN BY BRACKETS AND UNDERLINING

1. (Twice Amended) Transdermal therapeutic system comprising a backing layer, at least one nicotine-containing layer or zone, and [at least one essential] an additive comprising spearmint oil [extracted from a mint species] or at least one monoterpene ketone contained in [said essential oils] spearmint oil, wherein the content of at least one monoterpene ketone in the nicotine-containing layer or zone is 0.1 to 5.0%-wt of the weight of the layer or zone.

3. (Twice Amended) Transdermal therapeutic system according to claim 2, wherein the monoterpene ketone is a pure enantiomer thereof or a mixture of enantiomers thereof.

4. (Twice Amended) Transdermal therapeutic system according to claim 1, wherein the [essential oil is] additive comprises spearmint oil.

6. (Twice Amended) Process for masking an unpleasant smell, caused by the presence of nicotine, comprising adding to a nicotine-containing layer or zone of a nicotine-containing transdermal therapeutic system, [comprising adding] 0.1 to 5.0%-wt, based on the weight of the layer or zone, of at least one odor-improving substance [to the nicotine-containing transdermal therapeutic system], said

substance being [an essential] spearmint oil [extracted from a mint species] or [a] at least one monoterpene ketone contained in [an essential] spearmint oil [extracted from a mint species].

15. (Amended) Transdermal therapeutic system according to claim 5, wherein the content of the at least one monoterpene ketone in the nicotine-containing layer or zone is 0.5- 2%-wt of the weight of the layer or zone.

16. (Amended) Process according to claim [9] 6, wherein the at least one mototerpene ketone is added to the nicotine - containing layer or zone in a quantity constituting 0.5-2% wt of said layer or zone.